

AMENDMENTS TO THE CLAIMS

1. **(Currently amended)** A method of screening for an agent for inhibiting or reducing the proliferation or growth of lung cancer cells, comprising contacting ~~the lung cancer~~ cells with an amount of an agent ~~effective to inhibit or reduce the proliferation or growth of the lung cancer~~ cells, wherein the agent is a ~~pte~~ ptc therapeutic ~~and wherein the agent is a small organic molecule, and determining, as compared to a control, whether the agent which inhibits or attenuates hedgehog/patched signal transduction and whether the agent inhibits or reduces thereby inhibiting or reducing~~ cell proliferation or growth, wherein if the agent inhibits or attenuates the hedgehog/patched signal transduction and inhibits or reduces cell proliferation or growth relative to the control, then an agent that inhibits or reduces the proliferation or growth of lung cancer cells is identified ~~and wherein the agent is a small organic molecule.~~
2. **(Currently amended)** A method of screening for an agent for inducing the formation of, or the maintenance or functional performance of normal lung tissue, comprising contacting ~~the lung tissue~~ with an amount of an agent ~~effective to induce the formation of new lung tissue,~~ wherein the agent is a ~~pte~~ ptc therapeutic, and determining, as compared to a control, whether the agent that promotes hedgehog/patched signal transduction and whether the agent induces thereby inducing the formation of, or the maintenance or functional performance of normal lung tissue, wherein if the agent promotes hedgehog/patched signal transduction relative to the control and induces the formation of, or the maintenance or functional performance of normal lung tissue, then an agent that induces the formation of, or the maintenance or functional performance of normal lung tissue is identified.
3. **(Previously presented)** The method of claim 1, wherein the lung cancer cell is in culture, and the agent is provided as a cell culture additive.
4. **(Original)** The method of claim 1, wherein the cell is treated in an animal and the agent is administered to the animal as a therapeutic composition.

5. **(Withdrawn)** The method of claim 1, wherein the agent is a hedgehog therapeutic.
6. **(Withdrawn)** The method of claim 5, wherein the hedgehog therapeutic is a polypeptide including a hedgehog polypeptide sequence of at least a bioactive extracellular portion of a hedgehog protein.
7. **(Withdrawn)** The method of claim 6, wherein the polypeptide includes at least 50 amino acids residues of an N-terminal half of the hedgehog protein.
8. **(Withdrawn)** The method of claim 6, wherein the polypeptide includes at least 100 amino acids of an extracellular domain of the hedgehog protein.
9. **(Withdrawn)** The method of claim 6, wherein the polypeptide includes at least a portion of the hedgehog protein corresponding to a 19kd fragment of an extracellular domain of the hedgehog protein.
10. **(Withdrawn)** The method of claim 6, wherein the hedgehog protein is encoded by a gene of a vertebrate organism.
11. **(Withdrawn)** The method of claim 6, wherein the polypeptide includes a hedgehog polypeptide sequence represented in the general formula of SEQ ID No. 21.
12. **(Withdrawn)** The method of claim 6, wherein the polypeptide includes a hedgehog polypeptide sequence represented in the general formula of SEQ ID No. 22.
13. **(Withdrawn)** The method of claim 6, wherein the hedgehog protein is encoded by a human hedgehog gene.
14. **(Withdrawn)** The method of claim 6, wherein the hedgehog polypeptide sequence is at least 60 percent identical to an amino acid sequence of a hedgehog protein selected from SEQ ID

No:9, SEQ ID No:10, SEQ ID No:11, SEQ ID No:12, SEQ ID No:13, SEQ ID No:14, SEQ ID No:15, or SEQ ID No:16.

15. **(Withdrawn)** The method of claim 6, wherein the hedgehog polypeptide sequence is encodable by a nucleotide sequence which hybridizes under stringent conditions to a sequence selected from SEQ ID No:1, SEQ ID No:2, SEQ ID No:3, SEQ ID No:4, SEQ ID No:5, SEQ ID No:6, SEQ ID No:7, or SEQ ID No:8.

16. **(Withdrawn)** The method of claim 6, wherein the hedgehog polypeptide sequence is an amino acid sequence of a hedgehog protein selected from SEQ ID No:9, SEQ ID No:10, SEQ ID No:11, SEQ ID No:12, SEQ ID No:13, SEQ ID No:14, SEQ ID No:15, or SEQ ID No:16.

17. **(Withdrawn)** The method of claim 6, wherein the hedgehog polypeptide sequence is an amino acid sequence of a Sonic hedgehog protein.

18. **(Cancelled)**

19. **(Currently amended)** The method of claim 2, wherein the ~~pte~~ ptc therapeutic is a small organic molecule which binds to a patched protein and derepresses patched-mediated inhibition of mitosis.

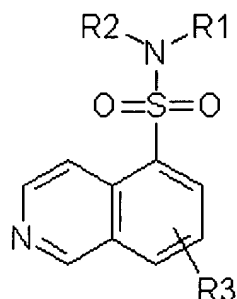
20. **(Currently amended)** The method of claim 2, wherein the ~~pte~~ ptc therapeutic binds to patched and mimics hedgehog, thereby promoting hedgehog/patched signal transduction.

21. **(Currently amended)** The method of claim 1 or 20, wherein the ~~pte~~ ptc therapeutic is a small organic molecule.

22. **(Currently amended)** The method of claim 2, wherein the ~~pte~~ ptc therapeutic is a protein kinase A inhibitor or a ptc antisense construct.

23. **(Currently amended)** The method of claim 22, wherein the protein kinase A inhibitor is selected from N-[2-((p-bromocinnamyl)amino)ethyl]-5-isoquinolinesulfonamide, 1-(5-isoquinoline-sulfonyl)-2-methylpiperazine, KT5720, ~~8-bromo-cAMP, dibutyl-cAMP~~ and PKA Heat Stable Inhibitor isoform α .

24. **(Previously presented)** The method of claim 22, wherein the protein kinase A inhibitor is selected from a molecule of Formula I



wherein R_1 and R_2 each can independently represent hydrogen, and as valence and stability permit a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl (such as a carboxyl, an ester, a formate, or a ketone), a thiocarbonyl (such as a thioester, a thioacetate, or a thioformate), an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, $-(CH_2)_m-R_8$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$ -lower alkyl, $-(CH_2)_m-O$ -lower alkenyl, $-(CH_2)_n-O-(CH_2)_m-R_8$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$ -lower alkyl, $-(CH_2)_m-S$ -lower alkenyl, $-(CH_2)_n-S-(CH_2)_m-R_8$, or

R_1 and R_2 taken together with N form a heterocycle (substituted or unsubstituted);

R_3 is absent or represents one or more substitutions to the isoquinoline ring such as a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl (such as a carboxyl, an ester, a formate, or a ketone), a thiocarbonyl (such as a thioester, a thioacetate, or a thioformate), an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, $-(CH_2)_m-R_8$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$ -lower alkyl, $-(CH_2)_m-O$ -lower alkenyl, $-(CH_2)_n-O-(CH_2)_m-R_8$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$ -lower alkyl, $-(CH_2)_m-S$ -lower alkenyl, $-(CH_2)_n-S-(CH_2)_m-R_8$;

R₈ represents a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl, or heterocycle; and

n and m are independently for each occurrence zero or an integer in the range of 1 to 6.

25. **(Previously presented)** The method of claim 1, wherein the lung cancer cells are small cell lung cancer (SCLC) cells or non-small cell lung cancer (NSCLC) cells.

26. **(Previously presented)** The method of claim 1, wherein the lung cancer cells are adenocarcinoma cells, lung cell carcinoma cells, or squamous cell carcinoma cells.